Table1. 4-year changes (mean [95%CI]) in anatomical cross-sectional areas and (specific) strength

	Anatomical cross-sectional areas		Strength	Specific Strength	
	Hamstrings	Adductors	Flexors	Extensors	Flexors
Chronically painful(n=30)	-4.6[-6-5/-2.7]*	-4.0[-8.7/16.6]	+3.8[-13.2/20.8]	+3.8[-11.8/19.4]	+9.1[-8.2/26.4]
Painless(n=30)	-3.3[-5.6/-1.0]*	+2.5[-7.7/15.5]	-16.4[-26.3/-7.3]*	+5.5[-10.7/21.7]	-14.0[-23.7/-4.4]*

*p for change over 4 years $\leq$ 0.01

573

SUBCHONDRAL TRABECULAR BONE MORPHOLOGY CHANGES FOLLOWING ACL INJURY: A MATCHED CASE-CONTROL STUDY

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Purpose: There is limited information available regarding changes in tibial trabecular bone morphology that occur within the subacute phase (<6 months) following ACL injury, or how these values change over time after reconstructive surgery. Additionally, there is a substantial void in the literature regarding normal tibial Fractal Signature Analysis (FSA) values in healthy, non-injured adults, making interpretation of FSA values in injured subjects challenging. Consequently, the purpose of this investigation was to evaluate differences in medial and lateral tibial FSA values following ACL injury and describe how these values change over time following ACL-reconstruction in subjects with normal, as well as narrowed tibiofemoral Joint Space Width (JSW) compared to controls.

Methods: A prospective cohort study design was used to evaluate 32 first-time, acute ACL-injured subjects (18 women), as well as 32 healthy controls (18 women) matched by sex, age, BMI, and activity level. Entry criteria for injured subjects included: Age 14-55yrs; BMI = 18.5-30, Tegner score $\geq$ 5; no previous knee pathologies; normal clinical knee exam, normal anatomic alignment; < 2/3 menisectomy; < Gr IIIb articular cartilage lesions (Int. Knee Documentation Committee (IKDC) grading criteria). Similar entry criteria were employed for controls with the addition of normal MRIs at baseline and final follow-up. Bilateral anterior-posterior (AP) view x-rays were obtained from all subjects using a semi-flexed, metatarsal phalangeal (MTP) view technique at baseline (pre-surgery for ACL-injured subjects) as well as 2 and 4 years post ACL-reconstruction (ACL-R). Medial and lateral compartment FSA was performed using commercially available software (KneeAnalyzer, Optasia Medical, Manchester, UK). Mixed model repeated measures analyses of variance and covariance adjusted for age, sex, activity level, and time since injury (for cases) were used to test three hypotheses: 1) There are no significant differences in bilateral FSA values for ACL-injured subjects or controls at pre-surgical baseline. 2) Side-to-side differences in mean FSA values do not change significantly over time in ACL-R subjects or controls. And 3) ACL-R subjects with significantly narrowed tibiofemoral JSW at final follow-up have significantly decreased mean side-to-side FSA values compared to ACL-R subjects with normal JSW as well as controls.

Results: Results of analyses evaluating bilateral differences in mean Horizontal and Vertical fractal dimensions (FD) for each hypothesis are presented in Table 1. There were no statistically significant side-to-side differences in medial or lateral FSA values at baseline for ACL-injured, or control group subjects, and these values did not change significantly over time within either group (hypothesis 1). Significant differences were found for mean lateral compartment horizontal FD change over time between control and ACL-reconstructed subject groups, through the group by time interaction ($p = 0.035$), with control values increasing over time and cases decreasing (hypothesis 2). Subgroup FSA comparisons between ACL-R subjects with normal JSW and those with narrowed JSW (at final follow-up) as well as controls revealed a significant group by time interaction effect ($p = 0.04$) for lateral compartment vertical FD change over time, with ACL-R narrowed JSW subjects significantly increasing compared to ACL-R normal JSW subjects ($p = 0.01$; hypothesis 3).

Conclusions: To our knowledge, these data represent the first side-to-side medial and lateral FSA values in healthy controls. With no significant side-to-side differences, these findings provide a rationale to use the healthy contralateral knee as a control for the injured knee in future studies. Furthermore, our analyses reveal significant changes in lateral FD values for ACL-injured knees compared bilaterally, as well as when comparing ACL-R subjects with normal- and narrowed-JSW over time. Decreased mean horizontal FD values over time in injured subjects compared to controls suggests thickening of subchondral trabeculae in these subjects. These lateral compartment findings correspond with additional changes observed within this cohort, such as tibiofemoral Joint Space Width Differences at baseline and follow-up. These findings are a novel contribution and are a first step in understanding how early changes in subchondral bone may contribute to the post-traumatic OA process. Further research is required to elucidate the etiology of changes in bone in PTOA.

Table 1
FSA Side-to-Side differences in mean Fractal Dimensions (FD) at baseline and over time (p-values).

			Medial		Lateral	
			Horizontal FD	**Vertical FD**	**Horizontal FD**	**Vertical FD**
Hypothesis 1 (adjusted for age, sex, activity level, and time since injury)	Baseline side-to-side FSA differences within each group, group effects	**Controls**	0.74	0.97	0.73	0.55
		Cases	0.49	0.45	0.33	0.86
	Change in side-to-side FSA difference values over time within each group, time effects	**Controls**	0.93	0.06	0.08	0.65
		Cases	0.38	0.77	0.11	0.99
Hypothesis 2 (adjusted for age, sex, and activity level)	Differences between ACL-R Cases and Controls over time, group by time interaction effects.		0.37	0.59	**0.035***	0.83
Hypothesis 3 (adjusted for age, sex, and activity level)	Differences between JSW groups (ACL-R Narrowed, and Normal JSW) and controls over time, group by time interaction effects.		0.53	0.21	0.12	**0.04***